Comparison of the Effect of Intraoperative 1 mg/kg/h and 2 mg/kg/h IV Lidocaine Infusion on Postoperative Pain and Nausea-Vomiting in Laparoscopic Gastric Bypass Surgery

Objective: *To relieve postoperative pain and nausea and vomiting, various drugs and methods, including intraoperative IV lidocaine infusion in different surgeries. However, the exact same dose has not yet been determined. The purpose of this study was to evaluate and compare the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on postoperative pain and nausea-vomiting in laparoscopic gastric bypass surgery.*
Methods: *This clinical trial study was performed on patients undergoing laparoscopic gastric bypass surgery in Rasoul-e-Akram Hospital, Iran. Patients were randomly assigned into two groups (1 mg/kg/h lidocaine) and (2 mg/kg/h lidocaine). Postoperative pain and nausea and vomiting were evaluated at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after surgery. Data was analyzed using statistical tests and SPSS 22.*
Results: *There was no significant difference in the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on static and dynamic pain and nausea-vomiting, agitation, systolic BP, diastolic BP, pulse rate and postoperative administration of pethidine in laparoscopic gastric bypass (P>0.05).*
Conclusion: *Based on results of this study, administration of low dose lidocaine (1 mg/kg/h) can be considered as an appropriate dose of IV lidocaine infusion in order to control postoperative pain and nausea and vomiting in laparoscopic gastric bypass surgery.*

Keywords: lidocaine, pain, nausea-vomiting, gastric bypass

1. Introduction

In post-operative time, it is important to control and reduce postoperative pain and nausea-vomiting (1). Different drugs and methods are used to relieve postoperative pain and nausea and vomiting in different surgeries (2). One of these methods, which has been studied on numerous occasions, is intraoperative intravenous (IV) lidocaine infusion undergone in a wide range of surgical procedures such as laparotomy, laparoscopy, gynecological surgery, orthopedics, etc., and has a positive effect in most cases in reducing postoperative pain and nausea-vomiting (3). Considering the pharmacological effects of IV lidocaine, which has both anti-inflammatory and anti-analgesic effects (protein receptor inhibitor G and NMDA), lidocaine has been used to relieve postoperative pain (4). According to numerous studies on various surgical procedures, intraoperative IV lidocaine infusion has been shown to reduce postoperative pain and nausea and vomiting (5-14). Although the exact same dosage is still unknown, the conducted studies have used 1-2 mg/kg/h dosages. In a double-blind clinical

trial on 41 patients undergoing microdistomy in two groups receiving 1.5 mg/kg/h lidocaine infusion and normal saline infusion as placebo, Kim et al (2014) concluded that fentanyl administration and postoperative pain intensity were significantly lower in the lidocaine group except 48 hours after surgery. Total fentanyl administration, hospital stay and satisfaction were significantly lower in lidocaine group than placebo group. Finally, intraoperative systemic infusion of lidocaine reduces pain level during microdistomy surgery (6). According to the studies, this study tends to evaluate and compare the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on postoperative pain and nausea-vomiting in laparoscopic gastric bypass to determine a more suitable and effective dosage.

2. Materials and Methods

This study was a randomized clinical trial. The studied population included elective patients who were candidate for laparoscopic gastric bypass referred to Rasoul-e-Akram Hospital since June 2014 to March 2015. Sampling method was convenient sampling. Sample size was determined using Cohen table with 80% statistical power, 0.05 alpha and 0.9 accuracy (21 subjects in each group). This study was a randomized clinical trial. Block randomization was done in quadrilateral blocks. This study was performed on 42 elective patients who were candidate for laparoscopic gastric bypass referred to Rasoul-e-Akram Hospital since June 2014 to March 2015. After obtaining consent and qualifying patients for inclusion and exclusion, 41 patients were assigned into 2 groups of 21 patients (A and B) in 4 blocks. After entering the operating room, standardized monitoring (ECG-POM-NIBP-Etco2) and insertion of two 20G IV catheters and 3 cc/kg crystalloid serum infusion were performed for all patients. Then, 3 mcg/kg fentanyl based on TBW and 0.02 mcg/kg midazolam based on TBW were administered as premedication for all patients. For induction, all patients received 5 mg/kg thiopental sodium based on TBW followed by 0.2 mg/kg atracurium based on IBW and 1.5 mcg/kg bolus lidocaine based on IBW for general anesthesia. After intubation of the patients, all of them received 1.2 mac isoflurane followed by 0.03 mg/kg atracurium every 30 minutes and 50 mcg fentanyl every 40 minutes as maintenance. From the beginning of surgery, group A received 1 mg/kg/h IV lidocaine infusion and group B received 2 mg/kg/h IV lidocaine infusion by the pump until the end of surgery for a maximum of 4 hours. After the end of surgery and discontinuation of all drugs, patients were placed in reserve by 0.04 mg/kg nisosigine and 0.02 mg/kg atropine and extubation was done; patients were transferred

to PACU (recovery). The time to enter recovery was set at t=0; for 24 h, patients were monitored for pain based on numerical rating score (0-10), static and dynamic nausea-vomiting, blood pressure (BP), heart rate and agitation in predicted times in the recovery or surgery wards.

Finally, pain level was recorded in two A and B groups based on numerical rating score (0-10) at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after surgery.

Pain level was recorded in two A and B groups based on numerical rating score (0-10) at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after surgery. Static and dynamic nausea-vomiting was recorded in two A and B groups at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after surgery. Agitation was recorded in two A and B groups at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after surgery. Systolic BP, diastolic BP and heart rate were recorded in 2 groups A and B at times 0, 30 min, and 1 h after surgery.

Finally, data was analyzed by SPSS software version 22. In the analytical step, Kolmogorov-Sminov test was used for determining normality of quantitative values. Then, independent T-test or Mann-Whitney U-test were used for comparing the quantitative variables of two groups A and B. Chi-square test (Z) was used to compare the qualitative variables. Repeated measure ANOVA or Friedman test was used to check and compare the changes.

3. Results

In this study, 42 patients who were referred to surgery ward of the Rasoul-e-Akram Hospital in 2016 and underwent laparoscopic elective gastric bypass were enrolled in the study. In group A, 21 patients (50%) received intraoperative 1 mg/kg/h IV lidocaine infusion; in group B, 21 patients (50%) received intraoperative 2 mg/kg/h IV lidocaine infusion.

3.1. Determining and Comparing Pain in Two Groups A and B Based on Numerical Rating Score at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare the pain level in 2 groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass, the Mann-Whitney U-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of pain levels are summarized in Table 1.

Table 1: descriptive features and comparison of pain level in two groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (mean ± SD)	B (mean ± SD)		
0	1.67 ± 1.01	1.71 ± 0.78	0.014	0.989
30 min	2.67 ± 0.73	2.67 ± 0.65	0.139	0.889
1 h	3.29 ± 0.84	3.19 ± 0.98	0.346	0.729
6 h	5.71 ± 0.9	5.57 ± 1.2	0.898	0.369
12 h	4.86 ± 0.96	4.71 ± 0.95	0.404	0.687
24 h	3.95 ± 1.39	3.81 ± 1.03	0.199	0.842

Based on the results of Table 1, there was no significant difference between pain levels of patients in 2 groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass ($P>0.05$). There was a significant difference between pain levels of patients based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A ($P<0.001$, $X^2=94.18$). There was a significant difference between pain levels of patients based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group B ($P<0.001$, $X^2=88.29$).

3.2. Determining and Comparing Static Nausea-Vomiting in Two Groups A and B at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare static nausea-vomiting levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Frequency values and nausea-vomiting comparison are summarized in Table 2.

Table 2: descriptive features and comparison of static nausea-vomiting levels in two groups A and B after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (N, %)	B (N, %))		
0	2 (9.5%)	5 (23.8%)	1.26	0.896
30 min	4 (19%)	3 (14.3%)	0.4	0.655
1 h	0 (0%)	1 (4.8%)	0.22	0.587
6 h	0 (0%)	0 (0%)	0	0.5
12 h	0 (0%)	0 (0%)	0	0.5
24 h	0 (0%)	0 (0%)	0	0.5

Based on the results of Table 2, there was no significant difference between static nausea-vomiting levels of patients in 2 groups A and B at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass ($P>0.05$). There was a significant difference between static nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A ($P=0.01$, $X^2=15$). There was a significant difference

between static nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group B (P=0.008, X^2=15.73).

3.3. Determining and Comparing Dynamic Nausea-Vomiting in Two Groups A and B at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare dynamic nausea-vomiting levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Frequency values and nausea-vomiting comparison are summarized in Table 3.

Table 3: descriptive features and comparison of dynamic nausea-vomiting levels in two groups A and B after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (N, %)	B (N, %))		
0	8 (38.1%)	6 (28.6%)	0.65	0.742
30 min	14 (66.7%)	11 (52.4%)	0.95	0.828
1 h	5 (23.8%)	5 (23.8%)	0	0.5
6 h	0 (0%)	0 (0%)	0	0.5
12 h	0 (0%)	0 (0%)	0	0.5
24 h	0 (0%)	0 (0%)	0	0.5

Based on the results of Table 3, there was no significant difference between dynamic nausea-vomiting levels of patients in 2 groups A and B at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between dynamic nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A (P=0.001, X^2=45). There was a significant difference between dynamic nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group B (P=0.001, X^2=33.77).

3.4. Determining and Comparing Agitation in Two Groups A and B at Times 0, 30 min and 1 h after Surgery

In order to compare agitation levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min and 1 h after surgery in each of the two groups A and B (separately). Frequency values and agitation comparison are summarized in Table 4.

Table 4: descriptive features and comparison of agitation levels in two groups A and B after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (N, %)	B (N, %))		
0	6 (28.6%)	5 (23.8%)	0.35	0.636
30 min	5 (23.8%)	6 (28.6%)	0.35	0.636
1 h	1 (4.8%)	1 (4.8%)	0	0.5

Based on the results of Table 4, there was no significant difference between agitation levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was no significant difference between agitation levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P=0.072, X^2=5.25). There was no significant difference between agitation levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.097, X^2=4.66).

3.5. Determining and Comparing Systolic BP in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare systolic BP levels in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test and Mann-Whitney U-test were used. Friedman test and repeated measure test were used for comparison of systolic BP levels at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of systolic BP are summarized in Table 5.

Table 5: descriptive features and comparison of systolic BP levels in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (mean ± SD)	B (mean ± SD)		
0	141.76 ± 13.68	141.9 ± 14.92	0.032	0.974
30 min	139.33 ± 13.13	139.43 ± 15.27	0.025	0.98
1 h	134.05 ± 11.38	136.48 ± 10.42	0.768	0.477

Based on the results of Table 5, there was no significant difference between systolic BP levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between systolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P<0.001, X^2=27.71). There was a significant difference between systolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.012, X^2=5.59).

3.6. Determining and Comparing Diastolic BP in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare diastolic BP levels in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test was used. Repeated measure test was used for comparison of diastolic BP levels at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of diastolic BP are summarized in Table 6.

Table 6: descriptive features and comparison of diastolic BP levels in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (mean ± SD)	B (mean ± SD)		
0	91.24 ± 8.24	93.05 ± 9.71	0.651	0.519
30 min	89.57 ± 9.3	91.19 ± 11.27	0.508	0.615
1 h	86.24 ± 9.54	89.14 ± 7.35	1.18	0.245

Based on the results of Table 6, there was no significant difference between diastolic BP levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass ($P>0.05$). There was a significant difference between diastolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A ($P<0.001$, $X^2=58.94$). There was a significant difference between diastolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B ($P=0.001$, $X^2=11.38$).

3.7. Determining and Comparing Heart Rate in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare heart rate in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test and Mann-Whitney test were used. Repeated measure test and Friedman test were used for comparison of heart rate at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of heart rate are summarized in Table 7.

Table 7: descriptive features and comparison of heart rate in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (mean ± SD)	B (mean ± SD)		
0	93.05 ± 7.32	96.86 ± 6.64	1.76	0.085
30 min	90.29 ± 6.66	92.86 ± 8.31	1.26	0.207
1 h	86.43 ± 6.47	88 ± 7.44	0.9	0.364

Based on the results of Table 7, there was no significant difference between heart rate of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass ($P>0.05$). There was a significant difference between heart rate of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A ($P<0.001$, $X^2=28.5$). There was a significant difference between heart rate of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B ($P=0.001$, $X^2=67.43$).

3.8. Determining and Comparing the First, Second and Third Pethidine Administrations in Two Groups A and B after Laparoscopic Gastric Bypass

In order to compare the first, second and third pethidine administrations in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Frequency values and comparison of the first, second and third pethidine administrations in groups A and B after laparoscopic gastric bypass are summarized in Table 8.

Table 8: descriptive features and comparison of the first, second and third pethidine administrations in two groups A and B after laparoscopic gastric bypass

Time	Group		Test statistic	p-value
	A (N, %)	B (N, %)		
1st	6 (28.6%)	11 (52.3%)	1.61	0.053
2nd	12 (57.1%)	8 (38%)	1.26	0.103
3rd	3 (14.3%)	1 (4.8%)	1.06	0.144

Based on the results of Table 8, there was no significant difference between the first, second and third pethidine administrations in 2 groups A and B after laparoscopic gastric bypass ($P>0.05$).

4. Discussion

According to the most important results of this study, there was no significant difference between the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on postoperative pain, static and dynamic nausea-vomiting, agitation, systolic BP, diastolic BP, heart rate and pethidine administration after laparoscopic gastric bypass. In both groups, intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion significantly increased pain 6 hours postoperatively and significantly decreased pain 24 hours postoperatively. Moreover, postoperative static and dynamic nausea-vomiting, agitation, systolic BP, diastolic BP and heart rate significantly decreased 0-24 hours after the surgery. Therefore, lidocaine seems to reduce postoperative pain and complications. However, high-dose and low-dose lidocaine has the same significant effect in reducing pain and complications after laparoscopic gastric bypass.

Postoperative pain not only causes physical and mental torment, but also increases the risk of side effects and delayed recovery. Therefore, it is important to eliminate emotional pain and stress to maintain comfortable recovery, reduce the incidence of postoperative cardiovascular complications and increase sooner discharge (15). It has been previously reported that preoperative IV lidocaine infusion can increase postoperative analgesic effects and accelerate early recovery; intraoperative continuous infusion can effectively prevent central hyperalergy

227 through the pain pathway (16). Lidocaine has an insignificant opioid-sparing property in
228 patients undergoing various surgical procedures (17, 18). Several mechanisms have been
229 suggested to explain the insignificant opioid-sparing effect of preoperative lidocaine. First,
230 lidocaine has anti-inflammatory properties which can minimize the pain caused by surgical
231 inflammation (19, 20). Second, lidocaine also can directly block the pathways of pain
232 conducting sodium channels (21). Eventually, lidocaine can reduce the need for opioid drugs
233 or intraoperative volatile anesthetics, which may reduce the progression of postoperative pain
234 (22, 24).
235 Based on literature review, this study was the first study to compare the effects of two
236 different doses of lidocaine (1 mg/kg/h vs. 2 mg/kg/h IV infusion) on postoperative pain and
237 nausea-vomiting after laparoscopic gastric bypass. However, many studies have shown that
238 different doses of lidocaine infusion reduced postoperative pain level and side effects,
239 compared with placebo and other drugs. For example, Tikuišis et al (2014) studied 64
240 patients undergoing laparoscopic colon surgery and found that pain level significantly
241 decreased 24 h after the surgery in both rest and movement in 2 mg/kg/h lidocaine group
242 compared to placebo group. Moreover, there was no significant difference between
243 postoperative complications between the two groups (5). Through a meta-analysis, Ventham
244 et al. (2015) reviewed 40 clinical trials on comparing the effect of lidocaine infusion with
245 placebo or routine postoperative laparoscopic treatments and found that lidocaine
246 intervention reduced the pain score at rest in 2, 12 and 24 hours after surgery and reduced
247 nausea and vomiting (9). … et al (2015) studied 226 patients undergoing laparoscopic
248 gynecological surgery and rev[illegible]d that 1% lidocaine infusion was more effective on
249 postoperative pain than placebo (12). Terkawi et al (2016) found no significant difference in
250 pain scores between the two groups by follow-up of 216 patients after 2 days of abdominal
251 surgery in two groups of 1 mg/kg/h IV Lidocaine infusion and epidural analgesia. In
252 lidocaine group, episodes of hypotension and postoperative nausea and vomiting were less
253 frequent than placebo group (14).
254 In the above studies, pain and nausea-vomiting were not compared between two groups of 1
255 mg/kg/h and 2 mg/kg/h lidocaine; positive effect of lidocaine in reducing pain and nausea-
256 vomiting in most of these studies may be due to the fact that lidocaine has been compared
257 with opiate and placebo. Moreover, inconsistency of this study with some studies may be due
258 to differences in samples, design of studies, lidocaine doses and surgical site and procedures.
259 In the present study in which patients were carefully monitored for up to 24 hours after
260 surgery, although administration of high-dose lidocaine did not cause side effects after

surgery, administration of low doses, as high doses, reduced pain, nausea-vomiting and agitation. Therefore, low doses of lidocaine (1 mg/kg/h), rather than high doses (2 mg/kg/h), can be used as an appropriate dose of IV lidocaine infusion to control postoperative pain and nausea-vomiting in laparoscopic gastric bypass.

5. Conclusion

Based on the results of this study, low doses of lidocaine (1 mg/kg/h), rather than high doses (2 mg/kg/h), can be used as an appropriate dose of IV lidocaine infusion to control postoperative pain and nausea-vomiting in laparoscopic gastric bypass.

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